

U.S.S.N. 07/586,534
Filed: September 21, 1990
SECOND AMENDMENT AND RESPONSE TO OFFICE ACTION

SUB

(c) determining the three-dimensional structure of the targeted RNA, including the position of the critical site relative to the major and minor grooves;

(d) determining the sequence of nucleotides and structure flanking the critical site in the targeted ribonucleic acid that is specific to the critical region of the ribonucleic acid to be inhibited and within the minor groove; and

(e) synthesizing compounds that will bind specifically to the critical site within the minor groove of the targeted ribonucleic acid.

3. The method of claim 1 wherein the ribonucleic acid is selected from the group consisting of mRNA, rRNA, tRNA and viral RNA.

4. The method of claim 1 further comprising synthesizing compounds that inhibit protein synthesis from the targeted ribonucleic acid.

5. The method of claim 4 wherein protein synthesis is inhibited in cells selected from the group consisting of tumor cells, virally infected cells, and bacteria.

6. The method of claim 1 wherein the three-dimensional structure is modeled using sequences of the RNA and calculating the minimum energies for these structures.

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SUB
M
C

7. The method of claim 1 wherein the critical region of the targeted ribonucleic acid is determined by mutation of regions of the targeted RNA and analysis of the amino acid sequence derived from the mutated RNA.

8. The method of claim 1 wherein the targeted RNA is a tRNA, wherein the critical region of the tRNA is determined by site directed mutation of the tRNA and analysis of the function of the mutated tRNA.

9. The method of claim 1 further comprising determining an effective amount of the inhibitory compound and combining the inhibitory compound with a pharmaceutical carrier.

10. The method of claim 9 wherein the carrier is selected from the group consisting of retroviral vectors, pharmaceutically acceptable compositions for topical administration, pharmaceutically acceptable compositions for parenteral administration, pharmaceutically acceptable compositions for enteral administration, and combinations thereof.

Sub
I
C

11. (Amended) A compound specifically binding to and inhibiting the function of a targeted RNA molecule, wherein the compound is specifically directed to a critical region of the RNA molecule, located [with] within the minor groove of the RNA molecule, by a combination of the primary, secondary and tertiary structure of the critical region.

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C1/C2
~~12. (Amended) The compound of claim 11 wherein the RNA is selected from the group consisting of mRNA, tRNA, [and] rRNA, and viral RNA.~~

Sub J1
~~13. The compound of claim 11 further comprising a pharmaceutically acceptable carrier selected from the group consisting of retroviral vectors, pharmaceutically acceptable compositions for topical administration, pharmaceutically acceptable compositions for parenteral administration, pharmaceutically acceptable compositions for enteral administration, and combinations thereof.~~

Sub J1
~~14. (New) The method of claim 3 wherein the critical site is in the minor groove of the acceptor stem of a tRNA molecule.~~

Sub J1
~~15. (New) The method of claim 14 wherein the tRNA molecule is tRNA^{Ala}.~~

C2
~~16. (New) The method of claim 15 wherein the critical site is the G3:U70 base pair.~~

Sub I3
~~17. (New) The compound of claim 12 wherein the compound binds to a critical region within the minor groove of the acceptor stem of a tRNA molecule.~~

Sub I3
~~18. (New) The compound of claim 17 wherein the tRNA molecule is tRNA^{Ala}.~~